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Effect of Obstruction on Longitudinal Left Ventricular Shortening in Hypertrophic Cardiomyopathy

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Objectives We investigated the cause of the midsystolic drop (MSD) in left ventricular (LV) ejection velocities that are observed with hypertrophic cardiomyopathy (HCM) and severe obstruction.

Background Dynamic obstruction is an important determinant of symptoms and adverse outcome. The MSD in velocity and flow occurs in patients with gradients >60 mm Hg. The nadir velocity in the LV occurs simultaneously with peak gradient.

Methods We studied 36 patients with obstructive HCM and an MSD and compared them with 15 patients with HCM and no obstruction and with 25 age-matched normal control subjects. We measured LV ejection velocity proximal and distal to LV obstruction as well as tissue Doppler velocities and time intervals.

Results The duration of contraction of both the septum and lateral wall is shorter in obstructed patients with the MSD than in nonobstructed HCM patients: septal contraction 203 ± 68 ms vs. 271 ± 41 ms ($p < 0.001$). Parallel reduction in the length of shortening was noted: 1.2 ± 0.6 cm vs. 1.9 ± 0.4 cm ($p < 0.001$). The ejection velocity nadir follows the septal and lateral peak velocities by 100 ms and 60 ms, respectively. The velocity nadir occurs as both walls rapidly decelerate to their premature termination: septal deceleration 79 ± 35 cm/s^2 vs. 48 ± 21 cm/s^2 ($p < 0.001$). With medical abolition of obstruction the MSD disappears and the duration and length of contraction normalizes.

Conclusions These data indicate that the MSD is caused by premature termination of LV segmental shortening and is a manifestation of systolic dysfunction. (J Am Coll Cardiol 2007;49:1203–11) © 2007 by the American College of Cardiology Foundation

Evidence of left ventricular (LV) systolic dysfunction in obstructive hypertrophic cardiomyopathy (OHCM) has been difficult to detect, even when severe outflow tract obstruction is present. Ejection time is increased, an abnormality that has been attributed to obstruction because such prolongation occurs in valvular aortic stenosis but has not been observed in nonobstructive hypertrophic cardiomyopathy (NOHCM) (1). Yet, conventional LV ejection fraction (EF) often is actually increased in OHCM (2). Recently a midsystolic drop (MSD) in Doppler LV ejection velocity of >50% has been observed in patients with gradients >60 mm Hg, followed by a later second peak in velocity (3). Volumetric ejection flow has also been shown to decrease and then recover (4). The drop in Doppler velocity has been termed the "lobster claw abnormality" because of its typical appearance (3). In the present study we investigated the cause of the MSD by measuring longitudinal tissue Doppler imaging (TDI) velocities in HCM patients with severe obstruction, comparing them with nonobstructive patients and normal control subjects. We also evaluated the effect of medical abolition of severe gradients on LV flow velocity and tissue velocities.

Methods

Patients. Hypertrophic cardiomyopathy was diagnosed based on the 2-dimensional echocardiographic demonstration of a hypertrophied (wall thickness >15 mm) and nondilated LV in the absence of another cardiac or systemic disease capable of producing the magnitude of hypertrophy evident (5). From consecutive studies in 208 patients from the HCM clinic, 127 patients had obstructive HCM and 47 patients had high resting LV outflow tract (LVOT) gradients >60 mm Hg due to mitral-septal apposition and an MSD on pulsed or continuous-wave Doppler echocardio-

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Abbreviations and Acronyms

CW = continuous wave
EF = ejection fraction
HCM = hypertrophic cardiomyopathy
LV = left ventricle
LVOT = left ventricular outflow tract
MSD = midsystolic drop
NOHCM = nonobstructive hypertrophic cardiomyopathy
OHCM = obstructive hypertrophic cardiomyopathy
PW = pulsed wave
TDI = tissue Doppler imaging

graphy, as reported previously (3,4). We excluded 11 patients with left bundle branch block (LBBB), ventricular pacemaker, prior surgical septal myectomy, or poor quality echocardiograms not providing all the Doppler and TDI data required. The remaining 36 patients constituted the OHCM group. We compared these patients with 2 control groups. The NOHCM group consisted of 15 patients with NOHCM and matched LV wall thickness score (6), size, and EF. These patients had no demonstrable LVOT Doppler echocardiographic gradients at rest or after provocation with Valsalva's maneuver. An LVOT obstruction was defined as a peak instantaneous gradient >30 mm Hg. The control group consisted of 25 age- and gender-matched normal subjects with no history of cardiac disease who had normal resting echocardiograms and normal stress echocardiograms done for evaluation of atypical symptoms. In the course of their clinical care 15 patients from the OHCM group were given oral disopyramide to assess their clinical response; echocardiographic measurements were repeated 2.5 h later (7). Patients gave written consent to analysis of their echocardiograms and clinical information for research purposes as approved by the institutional review board of St. Luke's-Roosevelt Hospital Center.

Echocardiography. Studies were done using a commercially available system (Acuson Sequoia, Mountain View, California), with patients resting in left lateral decubitus position, and all recordings were acquired in midexpiration. Maximum LV wall thickness was assessed from the 2-dimensional echocardiogram, as previously described, and measurements of the end-diastolic wall thickness of the anterior septum, posterior septum, anterolateral wall, and posterior wall were made (6). Left atrial diameter and additional 2-dimensional measurements of LV end-systolic and end-diastolic volumes and LVEF were made according to guidelines (8,9).

Pulsed Doppler echocardiography. In OHCM patients, the MSD was recorded in the LV ejection flow stream 2 to 2.5 cm apical of the mitral valve, as previously described (3,4) (Fig. 1). For all pulsed-wave (PW) and continuous-wave (CW) Doppler measurements, the results of 3 tracings were averaged. The velocities and intervals measured are displayed in Figure 2.

Continuous-wave Doppler. In the OHCM patients, CW Doppler was used to measure LV outflow gradient (10). From the apical 5-chamber view the CW interrogating beam was placed through both the LV ejection flow and the LVOT jet. Small adjustments in beam angle allow visualization of both signals simultaneously. With medial positioning of the beam, mitral regurgitant flow was excluded. The LV MSD may be clearly visualized superimposed on the CW LVOT jet trace. The initial upslope and terminal downslope of the LV velocity trace are completely superimposable and congruent with the LVOT traces. The 2 traces diverge in early and then midsystole when LVOT traces rise and LV velocities fall (Figs. 2 and 3). There were 2 reasons why CW traces of the MSD were preferred to PW traces for comparisons between OHCM and control patients. First, the use of CW traces offers the opportunity for simultaneous measurement and comparison of LV and LVOT velocities, thus avoiding the errors introduced by sequential measurements. Second, velocity of PW traces in the LV increase as the sample volume approaches the plane of mitral-septal contact (11). Using CW velocities for comparisons obviates this spatial ambiguity, because CW MSD traces are highest modal velocities before the orifice.

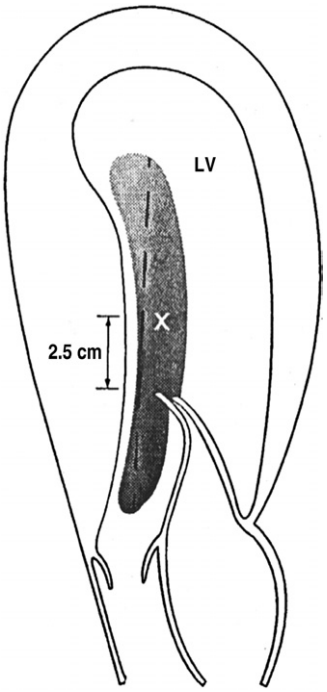

Figure 1 **Sampling Locations of PW and CW Doppler in the LV and LV Outflow Tract**

The midsystolic drop of left ventricular (LV) ejection velocity is recorded with pulsed-wave (PW) Doppler in the apical 5-chamber view with the sample volume placed approximately 2.5 cm apical to the level of the tips of mitral leaflets **(X)**. The continuous-wave (CW) Doppler **(dashed line)** traverses both the LV outflow tract and the medial LV cavity; velocities from both sites are recorded simultaneously.

Graphic representation of the velocities and intervals measured are displayed in Figure 2. Both the velocities and the intervals obtained with CW Doppler were compared with corresponding velocities and intervals obtained with PW Doppler.

TDI. Tissue Doppler velocities were recorded from the medial (septal) and lateral mitral annulus as previously reported (12). Aliasing velocities of 15 cm/s and sweep speed of 100

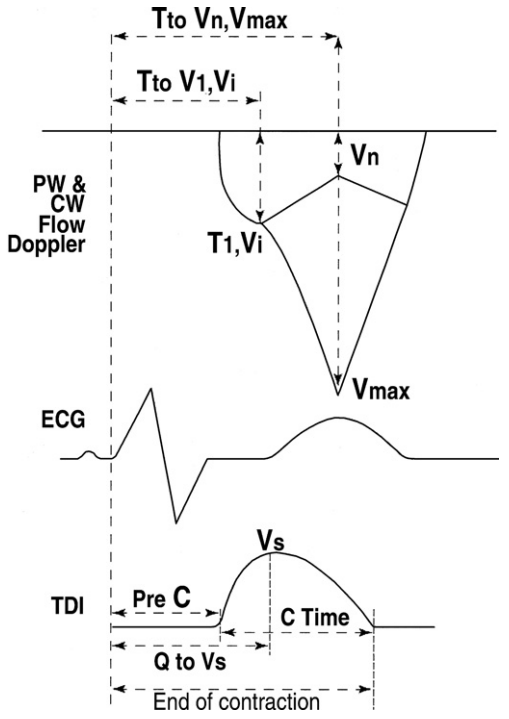

Figure 2 **Timing of the Midsystolic Drop in LV CW Velocities Compared With Timing of ECG and LV TDI**

Graphic depiction of continuous-wave (CW) Doppler of the superimposed left ventricular (LV) outflow tract and LV midsystolic drop velocities **(top)**, electrocardiogram (ECG) **(middle)**, and tissue Doppler imaging (TDI) traces of septal wall **(bottom)**. PW = pulsed-wave.

cm/s were used. Doppler gain was lowered until flow artifact was eliminated. The velocities and intervals measured are displayed in Figure 2. For comparison of pre- and post-disopyramide TDI velocities, measurements were also indexed for heart rate by dividing the measured intervals by their respective RR intervals (4).

Statistics. Paired and unpaired Student *t* tests and analysis of variance with Bonferroni correction were used to compare continuous variables. Three comparisons (OHCM, NOHCM, and control) were included in each Bonferroni adjustment. Chi-square tests compared categoric variables, and Fisher exact tests were used when the expected frequency was <5. Correlations were assessed with Pearson's correlation coefficients. A p value of 0.05 was considered statistically significant. The SPSS 10.0 software (SPSS, Chicago, Illinois) was used for statistical analyses.

Results

Demographic, clinical, and echocardiographic parameters of patients in the 3 groups are shown on Table 1. There were no differences in maximal LV wall thickness, LV volumes, EF, or New York Heart Association functional class between patients with OHCM and those with NOHCM. Also, maximal severity of mitral regurgitation among OHCM patients was moderate, and it did not correlate with any of the flow or TDI parameters.

Comparison of PW and CW Doppler of MSD. In the 76 patients, a total of 228 PW, 228 CW, and 304 TDI tracings were digitized and measured. Examples of the LV MSD recorded with CW and PW Doppler are shown in Figure 3. Correlations between the parameters of LV MSD velocities measured by pulsed and CW Doppler were excellent, as seen in Table 2. This validates the use of LV MSD velocities acquired by CW Doppler simultaneously with the LVOT jet velocities for subsequent analysis of MSD flow. The timing of the first velocity peak, V1 (at 0.2 ± 0.04 of total cycle duration), was simultaneous with the timing of inflection point, Vi (i.e., the point at which a normal convex outflow velocity curve becomes concave and abnormal ($r = 0.965$; $p < 0.0001$). The nadir of the MSD, Vn (at 0.32 ± 0.04 of cycle length), occurred simultaneously with peak outflow velocity: Vmax ($r = 0.999$; $p < 0.0001$). With CW Doppler, LV velocity dropped from V1 to Vn by 63% (from 2.5 ± 0.5 m/s to 0.9 ± 0.3 m/s; $p < 0.0001$). With PW Doppler, the drop in velocity was similar (59%).

CW Doppler flow and TDI results. The CW Doppler flow and TDI results are shown in Table 3. The heart rate was similar in all groups. Of the flow parameters, the patients with OHCM had, as expected, higher peak flow velocities, longer duration of ejection flow, and later peak in ejection velocity. In the OHCM patients, there was premature termination of shortening of both walls, resulting in decreased velocity time integral (VTI). Figure 4 compares TDI tracings of patients with NOHCM and those with OHCM. Premature termination of contraction was seen by a decrease in the absolute duration of contraction time (CTime) and, even more significantly, when expressed as ratio to corresponding ejection flow duration (CTime/ETime). As a consequence, calculated septal and lateral wall deceleration rate (rate of drop in contraction velocity) was significantly higher in OHCM patients than in NOHCM patients and control subjects (Table 3).

Flow and TDI after gradient reduction by medications. Fifteen patients with OHCM had LVOT gradient markedly reduced with medical treatment (Table 4). Besides near normalization of peak LVOT flow velocity, there was disappearance of the MSD. Also noted were expected findings that accompany successful negative inotropic therapy: prolongation of pre-ejection period and shortening of duration of ejection (ETime) and time to peak ejection velocity indexed to total ejection flow duration (TtoVmax/ETime). Tisue Doppler imaging after gradient abolition showed no changes in peak contraction velocities (Vs), but significant prolongation of CTime of both walls resulted in increased VTI in both septum and lateral walls. Figure 5 shows the post-treatment normalization of the ratio of contraction time to ejection time of both the septum and lateral wall.

In OHCM patients dyssynchronous delays are detected in the onset, peak, and end of lateral shortening compared with septal shortening, as shown in Table 5. In the extreme, 6 OHCM patients had >60 ms delay of onset lateral

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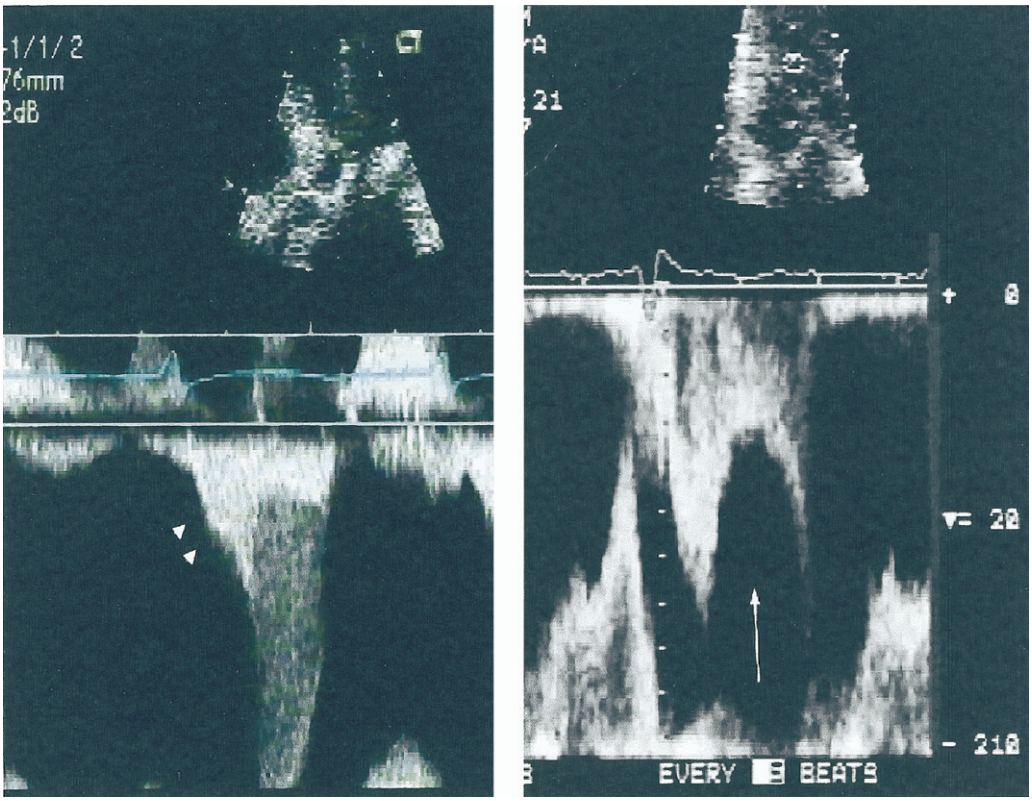

Figure 3 Midsystolic Drop in LV Velocity Seen on CW and PW Tracings

(Left) Continuous-wave (CW) Doppler through the left ventricular outflow tract (LVOT) in obstructive hypertrophic cardiomyopathy. The midsystolic drop (MSD) flow velocity curve **(arrowheads)** is seen superimposed on the higher LVOT ejection flow velocity signal. **(Right)** Pulsed-wave (PW) Doppler recording just apical of the entrance to the LVOT. **Long arrow** points to the nadir of LV MSD flow velocity.

shortening compared with onset septal shortening, and 6 patients had >60 ms delay in peak lateral shortening. After pharmacologic treatment, all of these delays are significantly reduced, as shown in Table 6.

Table 1 Demographic and Baseline Echocardiographic Data of Patients With OHCM, Patients With NOHCM, and Control Subjects

Variable	OHCM	NOHCM	Control	p Value
Age	61 ± 17	48 ± 13*	65 ± 18	0.008
Gender (M/F)	14/22	8/7	9/16	NS
NYHA functional class (I/II/III/IV)	2/4/22/8	5/6/4/0	25/0/0/0	0.0001
Maximal LV wall thickness	23.5 ± 3.1	22.6 ± 2.3	10.4 ± 1.3†	0.001
LVEF	0.81 ± 0.07	0.73 ± 0.14	0.65 ± 0.04‡	0.016
LVOT gradient (mm Hg)	132.3 ± 55.3	N/A	N/A	N/A
Beta-blockers (%)	64	60	52	NS
Calcium-channel blockers (%)	17	20	24	NS

*NOHCM versus both; †control versus both; ‡control versus OHCM.
LV = left ventricle; LVEF = left ventricular ejection fraction; LVOT = left ventricular outflow tract; NOHCM = nonobstructive hypertrophic cardiomyopathy; NYHA = New York Heart Association; OHCM = obstructive hypertrophic cardiomyopathy.

Graphic presentation. To present relationships between LV flow, LVOT flow, and septal and lateral wall TDI more graphically, we used pooled data from the 3 patient groups as well as the OHCM patients after pharmacologic gradient abolition to construct representative flow-TDI curves. These flow-TDI curves are presented in Figures 6 and 7. Figure 6 shows outflow and TDI velocities in normal control subjects (top) and NOHCM patients (bottom). Figure 7 shows curves

Table 2 Correlation of PW Doppler and CW Doppler Velocities and Time Intervals

Modality	Variable	PW Doppler	CW Doppler	r	p Value
Flow velocity (m/s)	V1	2.64 ± 0.56	2.45 ± 0.50	0.979	<0.001
	Vn	1.07 ± 0.37	0.91 ± 0.33	0.948	<0.001
	V2	1.77 ± 0.49	1.48 ± 0.40	0.893	<0.001
Time interval (ms)	PEP	83 ± 18	81 ± 17	0.873	<0.001
	Q to V1	164 ± 47	170 ± 42	0.908	<0.001
	Q to Vn	260 ± 60	264 ± 65	0.944	<0.001
	Q to V2	355 ± 60	351 ± 55	0.888	<0.001
	ETime	324 ± 46	323 ± 48	0.907	<0.001

CW = continuous-wave; ETime = ejection duration; PEP = pre-ejection period; PW = pulsed-wave; Q to V1 = time to first peak; Q to V2 = time to second peak; Q to Vn = time to nadir of midsystolic drop; V1 = first peak of left ventricular ejection velocity; V2 = second peak; Vn = nadir of the midsystolic drop.

Table 3 CW Doppler Flow and TDI Parameters in Patients With OHCM, Patients With NOHCM, and Control Subjects

Modality	Variable	OHCM	NOHCM	Control	p Value
CW Doppler	RR (ms)	862 ± 176	934 ± 191	966 ± 172	NS
	Vmax (m/s)	5.5 ± 1.1	1.5 ± 0.4	1.2 ± 0.2	<0.001
	PEP (ms)	89 ± 18*	104 ± 23	107 ± 16	0.003
	Q to Vmax (ms)	268 ± 53	199 ± 36	188 ± 37	<0.001
	ETime (ms)	330 ± 43	298 ± 44	299 ± 37	0.016
	Q to Vmax/ETime	0.54 ± 0.08	0.32 ± 0.08	0.27 ± 0.09	<0.001
Septal TDI	Septal Vs (cm/s)	9.5 ± 3.1	9.6 ± 1.7	10.9 ± 2.4	NS
	Septal VTI (cm)	1.2 ± 0.6	1.9 ± 0.4	2.0 ± 0.4	<0.001
	Septal PreCTime (ms)	105 ± 37	108 ± 28	104 ± 13	NS
	Septal Q to Vs (ms)	161 ± 45	178 ± 38	159 ± 26	NS
	Septal CTime (ms)	203 ± 68	271 ± 41	273 ± 40	<0.001
	Septal CTime/ETime	0.63 ± 0.19	0.91 ± 0.14	0.91 ± 0.12	<0.001
	Septal deceleration (cm/s^2)	78 ± 35	48 ± 21	52 ± 15	<0.001
Lateral wall TDI	Lateral Vs (cm/s)	11.5 ± 3.3	11.1 ± 2.1	11.3 ± 2.1	NS
	Lateral VTI (cm)	1.7 ± 0.5	2.3 ± 0.4†	1.8 ± 0.4	0.003
	Lateral PreCTime (ms)	135 ± 47	106 ± 26	116 ± 21	0.037
	Lateral Q to Vs (ms)	196 ± 65	185 ± 59	177 ± 38	NS
	Lateral CTime (ms)	238 ± 45	297 ± 64†	258 ± 35	0.002
	Lateral CTime/ETime	0.73 ± 0.14	1.0 ± 0.23	0.87 ± 0.14	<0.001
	Lateral deceleration (cm/s^2)	81 ± 35	52 ± 24	59 ± 22	<0.001

*OHCM versus Control; †NOHCM versus others.
CTime = duration of contraction; PreCTime = time to onset of contraction; Q to Vmax = time to peak ejection velocity; Q to Vs = time to peak contraction velocity; TDI = tissue Doppler imaging; Vmax = peak flow velocity; Vs = peak systolic tissue velocity; VTI = velocity time integral of systolic tissue velocity; other abbreviations as in Tables 1 and 2.

from patients with OHCM before (top) and after (bottom) medical abolition of the gradient. In Figure 7, top, note the simultaneous occurrence of V1 and the inflection point (Vi) on the LVOT tracing and simultaneous occurrence of Vmax and Vn. Note premature termination of both the septal and lateral TDI. Also note the delay in onset and delay in peak of contraction velocity of the lateral wall compared with the septum-systolic dyssynchrony. This delay disappears following successful abolition of LVOT gradient (Fig. 7, bottom).

Correlates of the LV MSD in ejection velocity. The slope of the MSD, the rate of drop in LV velocity from V1 to Vn, correlated significantly with the peak LVOT velocity (i.e., the LVOT gradient [$r = 0.520$; $p = 0.002$]). Duration of contraction of both septum and lateral wall correlated with the timing of Vn, indexed to ejection time ($r = 0.556$; $p = 0.0005$; and $r = 0.537$; $p = 0.007$; for septum and lateral wall, respectively).

Correlates of V1. The V1 correlates significantly with LVEF ($r = 0.495$; $p = 0.014$) and correlates negatively with LV end-systolic volume ($r = -0.422$; $p = 0.036$). When indexed to corresponding peak LVOT velocity (V1/Vmax), the correlation with LV end-systolic volume remained significant ($r = -0.407$; $p = 0.044$).

Discussion

In the present study we investigated the cause of the MSD in LV ejection velocities in patients with OHCM who have gradients >60 mm Hg. The principal findings were that in severe obstruction, when the MSD is present, the duration of LV longitudinal septal and lateral wall contraction is shortened; also, the extent (length) of longitudinal shortening is reduced, as assessed by the velocity–time integral, because of the premature truncation of shortening. Specifically, we found premature termination of systolic shortening in OHCM patients compared with control subjects without LV hypertrophy and compared with patients with NOHCM. Moreover, after medical abolition of LV outflow gradient, duration of contraction is prolonged and normalized and the MSD is no longer seen. The extent of the premature termination of shortening is particularly apparent when compared with the ejection time of flow (Fig. 7, top). The ratio CTime/ETime was only 0.63 for septum and 0.73 for lateral wall, emphasizing the premature termination of contraction. In contrast, this ratio was close to identity in normal subjects and NOHCM patients (Fig. 6).

The ejection velocity nadir follows the septal and lateral peak velocities by 100 ms and 60 ms, respectively. The flow nadir occurs as both walls rapidly decelerate to their premature termination (Fig. 7, top). Because of these observations—premature termination of shortening and normalization of both duration and extent of shortening after gradient abolition—we suggest that premature termination of longitudinal shortening is the primary cause of the MSD.

We also investigated the hypothesis that dyssynchrony of segmental contraction might contribute to the MSD. In OHCM there was an average 30-ms delay in the onset of lateral shortening that was not seen in NOHCM patients or in normal subjects. Six of these patients had delays of 60 ms or more. The delay in lateral shortening of the OHCM patients normalized after medical abolition of gradient. Though dys-

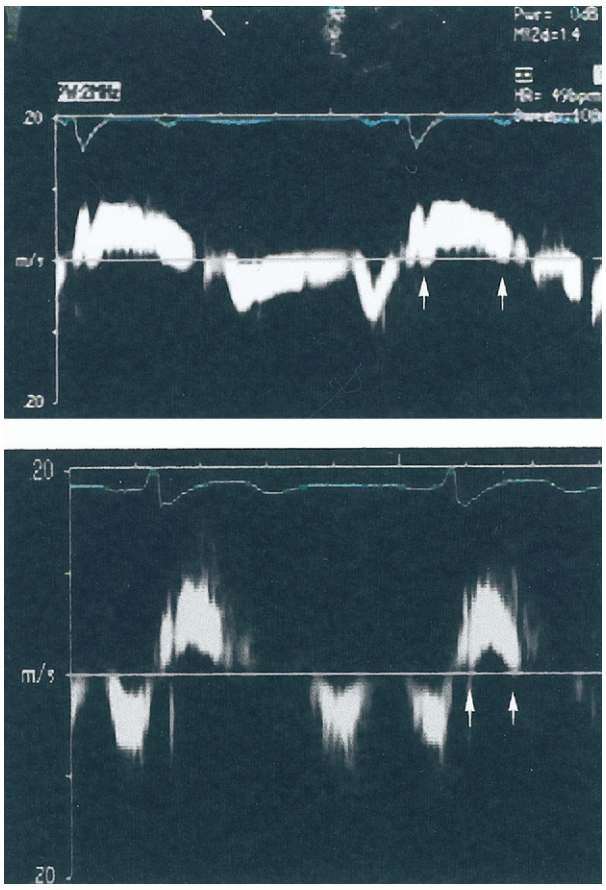

Figure 4 Septal TDI Tracing in Patient With Nonobstructive HCM Compared With Severe Obstructive HCM

(Top) Tissue Doppler imaging (TDI) tracing of a nonobstructed patient. **(Bottom)** TDI of a severely obstructed patient. Note the shortened duration of systolic septal contraction in the obstructed patient. The **white arrows** point to the beginning and the end of septal contraction, excluding the isovolumetric contraction. HCM = hypertrophic cardiomyopathy.

synchrony of segmental shortening may contribute to the MSD, we do not believe it is the primary sufficient cause, because we have not observed the MSD in patients with LBBB alone. Rather, when it occurs, systolic dyssynchrony may be a contributing cause to the MSD and may also cause diastolic dyssynchrony and diastolic dysfunction (13).

The midsystolic drop in LV ejection velocity. The midsystolic drop in LV ejection velocity is a prominent Doppler abnormality first observed on PW Doppler on the 5-chamber apical view in the LV, 2 to 2.5 cm apical of the mitral valve (3,4). In the present study, a >60% decrease occurred from first peak, V1, to the nadir. The MSD is only seen in patients with LVOT gradient >60 mm Hg (3). The LV flow is laminar during the MSD. It appears to be due to the sudden imposition of afterload caused by mitral-septal contact and the sudden development of rapidly increasing LVOT gradient (3,4,11,14). It cannot be due to mitral regurgitation, because it occurs on pulsed Doppler in the LV apical of the mitral valve. Previously, and in the present study, the timing of the nadir of the midsystolic drop has correlated temporally (at 0.32 of cycle length) exactly with the timing of peak LVOT gradient (peak afterload, the moment of maximum afterload mismatch) (3,4). The timing of V1 correlates with timing of mitral-septal contact (3,4). Moreover, not only Doppler velocity but also instantaneous descending and ascending aortic volumetric flow decreases in midsystole in patients with MSD (4,15,16). This MSD is the likely cause of midsystolic closure of the aortic valve seen on M-mode echocardiography and the "spike and dome" pulse tracing that was observed early after the initial description of OHCM.

At 0.20 of cycle length, the beginning of abrupt deceleration of flow velocity in the LV (V1) occurs simultaneously with the inflection point on the LVOT tracing (Vi) when the velocity curve abruptly shifts from convex to the left to concave to the left (Fig. 3, left, and Fig. 7, top). At this moment the pressure gradient itself starts to amplify obstruction (11), and the pressure gradient abruptly rises and the LV MSD begins, because afterload has exceeded LV segmental contractility.

Owing to continuity considerations, the fall in velocity in the LV body while the velocity is rising in the LVOT jet is only explained if the orifice progressively narrows after mitral-septal contact (3,4,11,14). Progressive orifice narrowing occurs because the mitral valve is pushed farther into the septum by the rising pressure difference across the mitral leaflet (11). Orifice narrowing during systole explains the concave-to-the-left contour of the LVOT jet velocity seen

Table 4 Doppler Parameters Before and After Gradient Abolition With Disopyramide

Modality	Variable	Pre-Disop	Post-Disop	p Value
CW Doppler	Vmax (m/s)	5.61 ± 1.05	2.1 ± 0.64	<0.001
	VTI (m)	1.01 ± 0.19	0.44 ± 0.13	<0.001
	PEP (ms)	91 ± 17	120 ± 23	<0.001
	T to Vmax (ms)	274 ± 56	255 ± 56	NS
	ETime (ms)	337 ± 51	298 ± 24	0.01
	T to Vmax/ETime	0.54 ± 0.08	0.45 ± 0.13	0.01
Septal TDI	Septal Vs (cm/s)	9.0 ± 2.8	8.6 ± 2.2	NS
	Septal VTI (cm)	1.14 ± 0.58	1.59 ± 0.53	0.01
	Septal PreCTime (ms)	109 ± 40	117 ± 34	NS
	Septal CTime (ms)	203 ± 66	248 ± 59	0.02
	Septal CTime/ETime	0.62 ± 0.21	0.83 ± 0.18	<0.001
Lateral wall TDI	Lateral Vs (cm/s)	10.8 ± 3.0	10.2 ± 2.3	NS
	Lateral VTI (cm)	1.6 ± 0.55	1.91 ± 0.52	0.05
	Lateral PreCTime (ms)	132 ± 51	115 ± 25	NS
	Lateral CTime (ms)	239 ± 43	280 ± 48	0.01
	Lateral CTime/ETime	0.72 ± 0.015	0.94 ± 0.14	<0.001

Disop = disopyramide; T to Vmax = time to peak LVOT flow velocity; other abbreviations as in Tables 1 to 3.

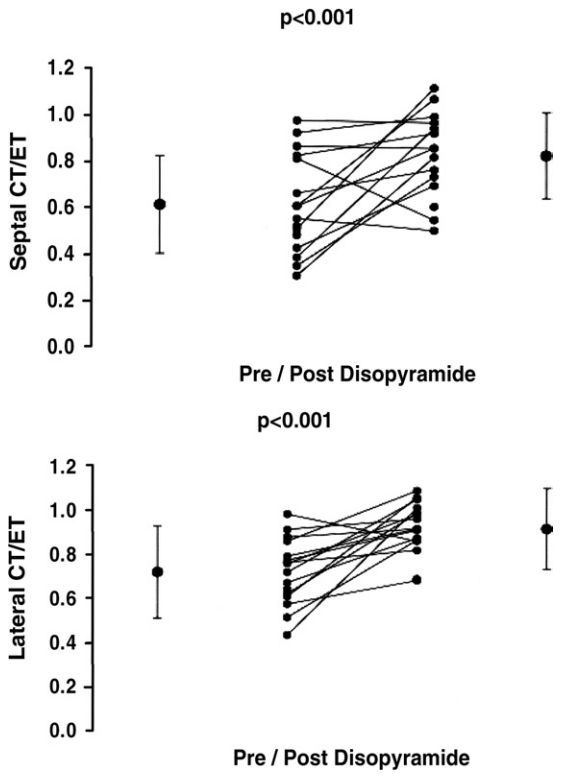

Figure 5 Increase in the Duration of Left Ventricular Contraction After Gradient Abolition

Change in normalized duration of contraction (ratio of contraction time duration to ejection flow duration [CT/ET]) of the septal **(top)** and lateral **(bottom)** walls in 15 individual patients after gradient abolition with disopyramide.

on CW Doppler. The orifice narrows because of the rise in the pressure difference; the pressure difference rises because of the decrease in the orifice. Obstruction begets further obstruction (3,11,14).

Qin et al. (17) found that although peak pressure gradient correlated with minimum orifice area, the peak LVOT flow rate appeared decreased by the reduction in the orifice. This reduction in volumetric flow rate was elegantly demonstrated by Conklin et al. (4), who found a negative correlation between peak gradient and flow rate. Moreover, they showed a further decrease in flow rate at peak gradient after dobutamine infusion. The increased afterload is sufficient to slow but not stop LV ejection. The authors pointed out that the MSD is a special case of afterload mismatch in which the LV is unable to maintain a normal instantaneous ejection volume against instantaneous increase in afterload (4,18).

Table 6 Lateral-Septal Delay in Onset of Contraction, Peak of Contraction Velocity, and End of Contraction in OHCM Patients Before and After Successful Gradient Abolition

	Pre-Gradient Abolition	Post-Gradient Abolition	p Value
Lateral-septal delay in pre-contraction time (ms)	51.7 ± 86.8	3.6 ± 42.8	0.015
Lateral-septal delay in time to peak contraction (ms)	66.1 ± 124.4	−0.71 ± 106.8	0.004
Lateral-septal delay in time to end of contraction	151.2 ± 176.0	29.6 ± 49.8	0.032

OHCM = obstructive hypertrophic cardiomyopathy.

Correlates of the MSD. Patients with higher V1 (contractility relative to load) had higher LVEF and smaller end-systolic volumes. The rate of deceleration from V1 is greater in patients with higher gradients. Patients with shorter contraction durations had earlier flow nadirs. The sequence of early systolic events described here is summarized as obstruction, premature termination of LV shortening, and deceleration of ejection flow.

The second peak. The second increase in flow occurs with a corresponding increase in orifice area (4). The LVOT gradient begins to fall because myocardial shortening velocities are declining or have prematurely terminated (Fig. 7, top). The second rise in flow and LV velocity occurs in parallel with the fall in the LVOT pressure gradient. The orifice reopens as the pressure gradient falls, just as it had narrowed with the rise in gradient (11).

Earlier data: myocardial velocities and afterload. In NOHCM, low-dose angiotensin II infusion, with a slight increase in afterload, caused a decrease in both systolic TDI velocities and ejection flow not detected in normal subjects (19). This model is different from the situation in dynamic LVOT obstruction, because the increase in afterload is not tonic throughout systole but occurs sharply after a period of unimpeded flow in early systole and is much higher than that induced with angiotensin II. Pellerin et al. (20) showed shortening of contraction time on pulsed TDI in patients with chronic coronary disease. We hypothesize that shortening of the duration of contraction may be one pattern of impaired contractility, either absolute or relative to afterload

Table 5 Dyssynchrony: Lateral-Septal Delay in Onset of Contraction, Peak of Contraction Velocity, and End of Contraction (in ms) in Patients With OHCM, Patients With NOHCM, and Control Subjects

	OHCM	NOHCM	Control	p Value
Lateral-septal delay in pre-contraction time (ms)	47.3 ± 87.2	−0.71 ± 38.2	16.6 ± 42.1	0.029*
Lateral-septal delay in time to peak contraction (ms)	54.1 ± 114.8	4.4 ± 83.6	27.3 ± 71.9	NS
Lateral-septal delay in time to end of contraction (ms)	113.6 ± 157.9	36.7 ± 146.8	10.2 ± 68.3	<0.001

*OHCM versus NOHCM.
Abbreviations as in Table 1.

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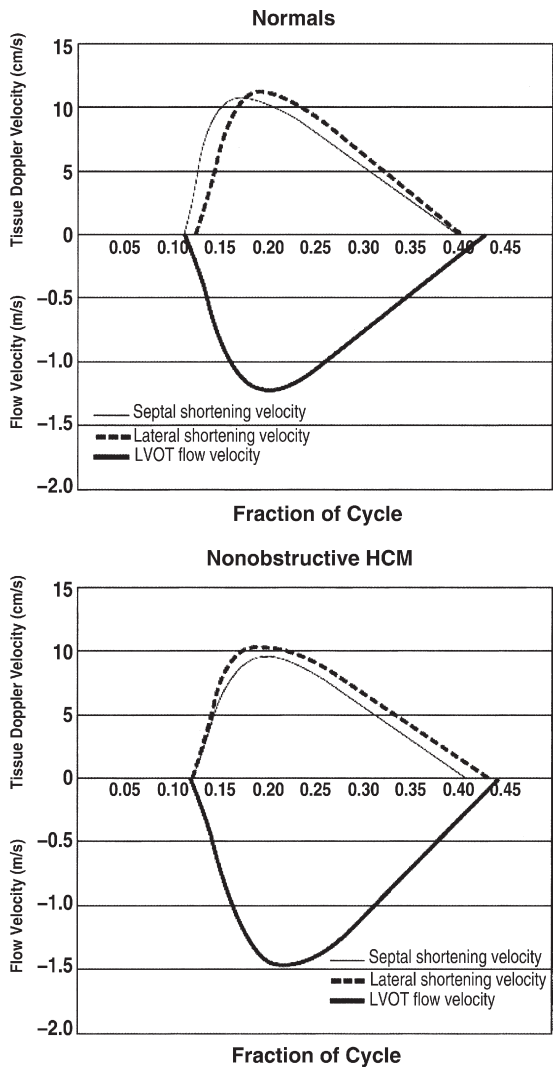

Figure 6 **Pooled CW Doppler and Tissue Doppler Data of Controls and Patients With Nonobstructive HCM**

(Top) Pooled data of normal controls. **(Bottom)** Pooled data from the nonobstructive patients. The septal and lateral tissue Doppler imaging (TDI) velocities are depicted above the zero velocity line, and the continuous-wave (CW) flow velocities are depicted below. Note that the TDI velocities and CW velocities are to different scales. HCM = hypertrophic cardiomyopathy; LVOT = left ventricular outflow tract.

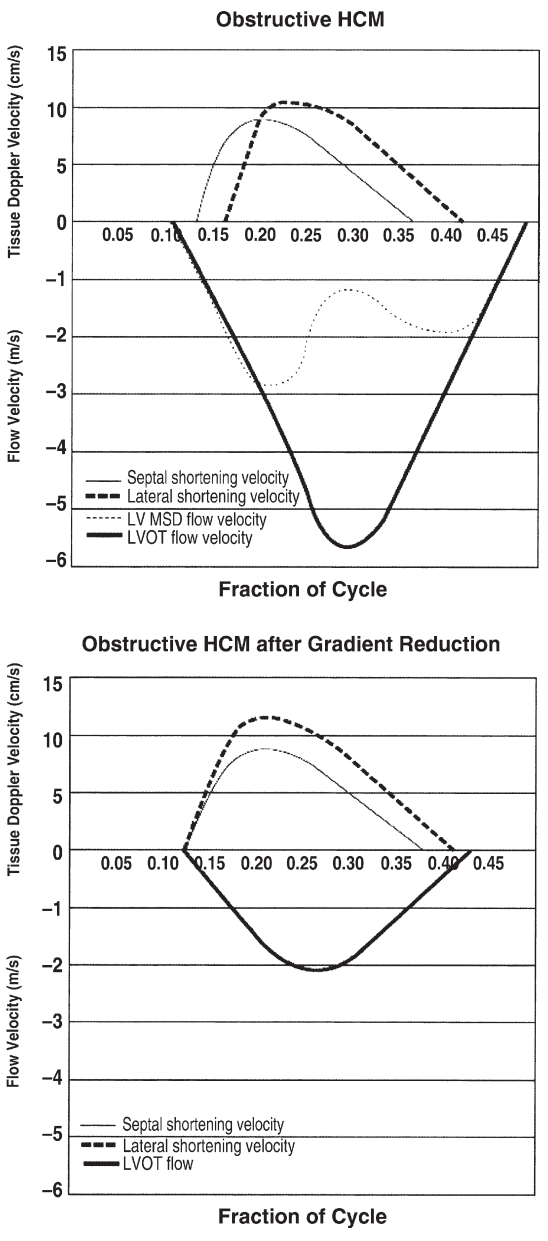

Figure 7 **Pooled CW and TDI Data in Obstructive HCM Before and After Gradient Abolition With Disopyramide**

The **top** graph shows the midsystolic drop of the left ventricular (LV) velocities **(dotted line)**, the premature termination of tissue Doppler imaging (TDI) velocities, especially relative to flow, and dyssynchrony of the septal and lateral wall shortening. The **bottom** graph shows significant improvement in these abnormalities after gradient abolition. CW = continuous-wave; HCM = hypertrophic cardiomyopathy; LVOT = left ventricular outflow tract; MSD = midsystolic drop.

mismatch as in our OHCM patients. The normalization of the duration of contraction after the obstruction is abolished with disopyramide supports this hypothesis. In addition, the constancy of Vs before and after disopyramide likely reflects the balanced negative inotropic and afterload-reducing effects of the intervention.

Study limitations. Although this was a retrospective study, we consecutively included all OHCM patients who had the MSD. It is thus representative of all patients with this abnormality of flow, which occurs in 84% of patients with gradients >60 mm Hg (3,4). Only shortening of the septal and lateral walls was examined in this study, but these observations sufficed to show both premature termination of shortening and dyssynchrony that were reversed by medical abolition of the gradient.

Implications and hypotheses. This study demonstrates for the first time an adverse effect of obstruction on LV systolic function. In patients with high gradients, obstruction causes premature termination of systolic shortening, the MSD in

LV ejection velocity, and decrease in instantaneous ejection flow (4).

The present data refute doubts about the adverse effect of the LVOT gradient on LV function (21). Rather than ending early (21), flow out of the LV occurs against the gradient, and is prolonged by the gradient (1,4,15,16). The apparent paradox of shorter contraction and prolonged flow is resolved by the understanding that it is the gradient that causes both.

We offer hypotheses that these phenomena may be felt in 2 important domains which suggest clinical investigations. First, because Conklin et al. (4) found a midsystolic fall in flow (and further decrease after gradient rise), these phenomena may impact heart failure symptoms by limiting increment in stroke volume after exertion (22,23). Second, we found significantly higher septal and lateral wall deceleration in MSD patients. We hypothesize that forced sudden termination of contraction with each beat may cause cumulative deceleration injury to the LV myocardium (24,25). This may contribute to symptoms and mortality associated with severe obstruction (1,26). In addition, in the present study we have shown that relief of obstruction completely prevents both the MSD in ejection velocities and the premature termination of contraction. Reversal of these adverse phenomena may contribute to the improved symptoms, hemodynamics, and survival that are observed after relief of obstruction (7,27,28).

Conclusions

The MSD in ejection velocities and flow are caused by premature termination of LV longitudinal segmental shortening.

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REFERENCES

1. Wigle D, Sasson Z, Henderson MA, et al. Hypertrophic cardiomyopathy. The importance of the site and the extent of hypertrophy. A review. Prog Cardiovasc Dis 1985;28:1–83.
2. Wigle ED, Rakowski H, Kimball BP, Williams WG. Hypertrophic cardiomyopathy—clinical spectrum and treatment. Circulation 1995; 92:1680–92.
3. Sherrid MV, Gunzburg DZ, Pearle G. Mid-systolic drop in left ventricular ejection velocity in obstructive hypertrophic cardiomyopathy, the lobster claw abnormality. J Am Soc Echocardiogr 1997;10: 707–12.
4. Conklin HM, Xiaoyan HH, Crispin DH, Sahn DJ, Shively BK. Biphasic left ventricular outflow and its mechanism in hypertrophic obstructive cardiomyopathy. J Am Soc Echocardiogr 2004;17:375–83.
5. Maron BJ. Hypertrophic cardiomyopathy: a systematic review. JAMA 2002;287:308–20.
6. Spirito P, Maron BJ, Bonow RO, Epstein SE. Occurrence and significance of progressive left ventricular wall thinning and relative cavity dilatation in hypertrophic cardiomyopathy. Am J Cardiol 1987;60:123–9.
7. Sherrid MV, Barac I, McKenna WJ, et al. Multicenter study of the efficacy and safety of disopyramide in obstructive hypertrophic cardiomyopathy. J Am Coll Cardiol 2005;45:1251–8.
8. Sahn DJ, DeMaria A, Kisslo J, Weyman A. Recommendation regarding quantitation in M-mode echocardiography: results of a survey of echocardiographic measurements. Circulation 1978;58: 1072–83.
9. Schiller NB, Shah PM, Crawford M, et al. Recommendations for quantitation of the left ventricle by two-dimensional echocardiography. J Am Soc Echocardiogr 1989;2:358–67.
10. Sasson Z, Yock PG, Hatle LK, Alderman EL, Popp RL. Doppler echocardiographic determination of the pressure gradient in hypertrophic cardiomyopathy. J Am Coll Cardiol 1988;11:752–6.
11. Sherrid MV, Chu CK, DeLia E, Mogtader A, Dwyer EM Jr. An echocardiographic study of the fluid mechanics of obstruction in hypertrophic cardiomyopathy. J Am Coll Cardiol 1993;22:816–25.
12. Garcia MJ, Rodriguez L, Ares M, et al. Myocardial wall velocity assessment by pulsed Doppler tissue imaging: characteristic findings in normal subjects. Am Heart J 1996;132:648–56.
13. Pak PH, Maughan WL, Baughman KL, Kass DA. Marked discordance between dynamic and passive diastolic pressure-volume relations in idiopathic hypertrophic cardiomyopathy. Circulation 1996;94:52–60.
14. Sherrid MV, Gunzburg DZ, Moldenhauer S, Pearle G. Systolic anterior motion begins at low left ventricular outflow velocity in obstructive hypertrophic cardiomyopathy. J Am Coll Cardiol 2000;36: 1344–54.
15. Gardin JM, Dabestani A, Glasgow GA, Butman S, Burn CS, Henry WL. Echocardiographic and Doppler flow observations in obstructed and nonobstructed hypertrophic cardiomyopathy. Am J Cardiol 1985; 56:614–21.
16. Maron BJ, Gottdiener JS, Arcce J, Rosing DR, Wesley YE, Epstein SE. Dynamic subaortic obstruction in hypertrophic cardiomyopathy: analysis by pulsed Doppler echocardiography. J Am Coll Cardiol 1985;6:1–15.
17. Qin JX, Shiota T, Lever HM, et al. Impact of left ventricular outflow tract area on systolic outflow velocity in hypertrophic cardiomyopathy: a real-time three-dimensional echocardiographic study. J Am Coll Cardiol 2002;39:308–14.
18. Ross J. Afterload mismatch in aortic and mitral valve disease: implications for surgical therapy. J Am Coll Cardiol 1985;5:811–26.
19. Mishiro Y, Oki T, Yamada H, et al. Use of angiotensin II stress pulsed tissue Doppler imaging to evaluate regional left ventricular contractility in patients with hypertrophic cardiomyopathy. J Am Soc Echocardiogr 2000;13:1065–73.
20. Pellerin D, Larraze F, Cohen L, Witchitz S, Veyrat C. Myocardial time intervals preceding left ventricular filling in chronic coronary artery disease: value of a decreased septal ejection time. Int J Cardiol 2003;89:33–44.
21. Murgo JP, Alter BR, Dorethy JF, Altobelli SA, McGranahan GM Jr. Dynamics of left ventricular ejection in obstructive and nonobstructive hypertrophic cardiomyopathy. J Clin Invest 1980;66:1369–82.
22. Lele SS, Thomson HL, Hiromi S, Belenkie I, McKenna WJ, Frenneaux MP. Exercise capacity in hypertrophic cardiomyopathy. Role of stroke volume limitation, heart rate and diastolic filling characteristics. Circulation 1995;92:2886–94.
23. Schwammenthal E, Schwarzkopff B, Block M, et al. Doppler echocardiographic assessment of the pressure gradient during bicycle ergometry in hypertrophic cardiomyopathy. Am J Cardiol 1992;69: 1623–8.
24. Fishman JE. Imaging of blunt aortic and great vessel trauma. J Thorac Imaging 2000;15:97–103.
25. Kaye P, O'Sullivan I. Myocardial contusion. Emergency investigation and diagnosis. Emerg Med J 2002;19:8–10.
26. Maron MS, Olivotto I, Betocchi S, et al. Effect of left ventricular outflow tract obstruction on clinical outcome in hypertrophic cardiomyopathy. N Engl J Med 2003;348:295–303.
27. Diodati J, Schenke W, Waclawiw MA, McIntosh CL, Cannon RO. Predictors of exercise benefit after operative relief of left ventricular outflow obstruction by the myotomy-myectomy procedure in hypertrophic cardiomyopathy. Am J Cardiol 1992;69:1617–22.
28. Ommen SR, Maron BJ, Olivotto I, et al. Long-term effects of surgical septal myectomy on survival in patients with obstructive hypertrophic cardiomyopathy. J Am Coll Cardiol 2005;46:470–6.